NOV 0 8 2004

I hereby certify that the presence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the

IPW

Docket No.: 28967/34891.1

(PATENT)

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Kari Alitalo et al.

Dated: November 4, 2004

Application No.: 10/774,802

10/774,802 Confirmation No.: 9059

Filed: February 9, 2004 Art Unit: 1646

For: ALT4 (VEGFR-3) AS A TARGET FOR

TUMOR IMAGING AND ANTI-TUMOR

THERAPY

Examiner: Not Yet Assigned

## **INFORMATION DISCLOSURE STATEMENT (IDS)**

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 CFR 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 CFR 1.97(b)(3)).

Copies of the references on the PTO/SB/08 are not provided since they were provided in related Application No. 09/169,079.

Application No.: 10/774,802 Docket No.: 28967/34891.1

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 13-2855, under Order No. 28967/34891.1. A duplicate copy of this paper is enclosed.

Dated: November 4, 2004

Respectfully submitted,

Eric M. Brusca

Registration No.: 52,664

MARSHALL, GERSTEIN & BORUN LLP

233 S. Wacker Drive, Suite 6300

**Sears Tower** 

Chicago, Illinois 60606-6357

(312) 474-6300

NOV 0 8 2004 &

Sub	estitute for form 1449A/B	J/PTO		Complete if Known		
				Application Number	10/774,802	
11	NFORMATIC	ON DIS	CLOSURE	Filing Date	February 9, 2004	
l s	TATEMEN1	BY A	PPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
	(Use as many sheets as necessary)			Examiner Name	To be Assigned	
Sheet	1	of	18	Attorney Docket Number	28967/34891.1	

			U.S. PA	TENT DOCUMENTS	
Examiner Initials*	Cite No.1	Document Number  Number-Kind Code <sup>2</sup> ( <i>if known</i> )	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	4,543,439	09/24/85	Fracketton, Jr. et al.	
	A2	4,652,639	03/24/87	Stabinsky	
	A3	4,933,294	06/12/90	Waterfield et al.	
	A4	5,183,884	02/02/93	Kraus et al.	
	A5	5,185,438	02/09/93	Lemischka	
	A6	5,198,359	03/30/93	Tanigucki et al.	
	A7	5,231,001	07/27/93	Kaplan et al.	
	A8	5,256,766	10/26/93	Coughlin	
	A9	5,270,458	12/14/93	Lemischka	· ·
	A10	5,283,354	02/01/94	Lemischka	
	A11	5,367,057	11/22/94	Lemischka	
	A12	5,635,177	06/03/97	Bennett et al.	
	A13	5,643,759	07/01/97	Pfreundschuh, M.	
	A14	5,693,762	12/02/97	Queen, C.L. et al.	
	A15	5,700,822	12/23/97	Hirth, K.P. et al.	
	A16	5,712,395	01/27/98	App, H. et al.	
	A17	5,747,651	05/05/98	Lemischka, I.R.	_
	A18	5,750,078	05/12/98	Shitara, K. et al.	
-	A19	5,763,441	06/09/98	App, H. et al.	
	A20	5,763,733	06/09/98	Whitlow, M. et al.	
	A21	5,776,427	07/07/98	Thorpe, P.E. et al.	
	A22	5,776,755	07/07/98	Alitalo, K. et al.	
•		5,798,097	08/25/98	McKenzie, I.F.C. et al.	
	A24	5,807,548	09/15/98	Shitara, K. et al.	
	+	5,952,199	09/14/99	Davis-Smyth et al.	
	A26	6,011,003	01/04/00	Charnock-Jones et al.	
	A27	6,331,302	12/18/01	Bennett, et al.	
	A28	6,451,764	09/17/02	Lee, et al.	

		FOREI	GN PATENT [	OCUMENTS	3		
Examiner	Cite	Foreign Patent Document	Publication Date	Name o	of Patentee or	Pages, Columns, Lines, Where Relevant Passages	
Initials*	No.1	Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)	MM-DD-YYYY	Applicant o	f Cited Document	or Relevant Figures Appear	
	B1	EP 0 325 224 A2	07/26/89 ·				
	B2	WO 90/14425	11/29/90				Γ'''
	B3	WO 92/13867	08/20/92				
	B4	WO 92/14748	03/09/92				
	B5	WO 93/14124	07/22/93				
	B6	WO 93/15201	08/05/93				
	B7	WO 94/10202	05/11/94				
	B8	WO 95/24473	09/14/95			_	
	B9	WO 95/33772	12/14/95				
	B10	WO 96/39515	12/12/96				
	B11	WO 97/05250	02/13/97				
	B12_	WO_97/09427	03/13/97				
	B13	WO 98/33917	08/06/98				
Examine	r				Date		
Signature	e				Considered		

Sub	stitute for form 1449A/B/PT	0		Complete if Known		
		_		Application Number	10/774,802	
II.	<b>IFORMATION</b>	I DI	SCLOSURE	Filing Date	February 9, 2004	
S	TATEMENT E	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
(Use as many sheets as necessary)			necessary)	Examiner Name	To be Assigned	
Sheet	2	of	18	Attorney Docket Number	28967/34891.1	

B14	WO 98/07832	02/26/98		
B15	WO 99/33485	07/08/99		

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
	C1	Achen, M.G. et al., "Vascular endothelial growth factor D (VEGF-F) is a ligand for the tyrosine kinases VEGF receptor 2 (Flk1) and VEGF receptor 3 (Flt4)," <i>Proc. Natl. Acad. Sci., USA, 95(2)</i> :548-553 (January, 1998).	
	C2	Achen, M.G. et al., "Monoclonal antibodies to vascular endothelial growth factor-D block its interactions with both VEGF receptor-2 and VEGF receptor-3," Eur. J. Biochem, 267(9):2505-15 (May, 2000).	
	СЗ	Andersson et al., "Structural and Functional Markers During Induced Differentiation in Human Leukemia Cell Lines," In R. F. Revoltella (ed.), Expression of Differentiated Functions in Cancer Cells. 239-245, Raven Press, New York (1982).	
	C4	Andre, T., et al., "Vegf, Vegf-B, Vegf-C and their receptors KDR, FLT-1 and FL the neoplastic progression of human colonic mucosa," <i>Int. J. Cancer</i> , 86(2):174-81 (April 15, 2000).	
	C5	Akagi, K., et al., "Vascular endothelial growth factor-C (VEGF-C) expression in colorectal cancer tissues," Br. J. Cancer, 83(7):887-91 (October, 2000).	
-	C6	Aprelikova et al., "FLT4, A Novel Class III Receptor Tyrosine Kinase in Chromosome 5q33-qter," Cancer Research, 52(3):746-748 (February 1, 1992).	
	C7	Aujame, L. et al., "High affinity human antibodies by phage display," Human Antibodies, 8(4):155-168 (1997).	
	C8	Beckstead, J.H. et al., "Evidence for the Origin of Kaposi's Sarcoma From Lymphatic Endothelium," Am. J. Pathol., 119(2):294-300 (May, 1985).	
	C9	Beers and Berkow eds. The Merck Manual of Diagnosis and Thereapy, Seventeenth Edition, pages 986-995, Merck & Co., Inc. Whitehouse Station, N.J., 1999.	
	C10	Berridge et al., "Cell-Lineage Antigens of the Stem Cell-Megakaryocyte-Platelet Linkage are Associated with the Platelet IIb-IIIa Glycoprotein Complex," Blood, 66(1):76-85 (July, 1985).	

Examiner	Date	
Signature	Considered	

Sub	stitute for form 1449A/B/PT	0		Complete if Known		
		_		Application Number	10/774,802	
IN	<b>IFORMATION</b>	I DI	SCLOSURE	Filing Date	February 9, 2004	
S	TATEMENT B	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
(Use as many sheets as necessary)		necessary)	Examiner Name	To be Assigned		
Sheet	3	of	18	Attorney Docket Number	28967/34891.1	

	C11	Bolen, J.B., "Nonreceptor Tyrosine Protein Kinases," <i>Oncogene</i> , 8:2025-2031 (1993).
	C12	Bolhuis, R.L. et al., "T cell targeting in cancer therapy," Cancer Immunology Immunotherapy, 34(1):1-8 (1991).
	C13	Borg et al., "Biochemical Characterization of Two Isoforms of FLT4, a VEGF Receptor-Related Tyrosin Kinase," Oncogene, 10:973-984 (1995).
	C14	Brown, L.F. et al., "Expression of Vascular Permeability Factor (Vascular Endothelial Growth Factor) and Its Receptors in Breast Cancer," Human Pathology, 26(1):86-91 (January, 1995).
	C15	Brüggemann, M. et al., "Production of human antibody repertoires in transgenic mice," Curr. Opin. Biotechnol., 8:455-458 (1997).
	C16	Brüggemann, M. et al., "Strategies for expressing human antibody repertoires in transgenic mice," <i>Immunol. Today, 17(8)</i> :391-397 (August, 1996).
	C17	Bunone, G., et al., "Expression of Angiogenesis Stimulators and Inhibitors in Human Thyroid Tumors and Correlation with Clinical Pathological Features," Am. J. Pathol, 155(6):1967-76 (December 1999).
	C18	Cantley et al., "Oncogenes and Signal Transduction," Cell, 64:281-302 (January 25, 1991).
	C19	Cao, Y., et al., "Vascular endothelial growth factor C induces angiogenesis in vivo," Proc. Natl. Acad. Sci. USA, 95:14389-94 (November 1998).
	C20	Carter, P. et al., "Toward the Production of Bispecific Antibody Fragments for Clinical Applications," <i>Journal of Hematotherapy</i> , 4:463-470 (1995).
	C21	Catoretti et al., "Monoclonal Antibodies Against Recombinant Parts of the Ki-67 Antigen (MIB 1 and MIB 3) Detect Proliferating Cells in Microwave-Processed Formalin-Fixed Paraffin Section," J. of Pathol., 168:357-363 (1992).
	C22	Cheng & Flanagan, "Identification and Cloning of ELF-1, a Developmentally Expressed Ligand for the Mek4 and Sek Receptor Tyrosine Kinases," <i>Cell</i> , 79:157-168 (October 7, 1994).
	C23	Cole et al., "The EBV-Hybridoma Technique and Its Application to Human Lung Cancer," Monoclonal Antibodies and Cancer Therapy, Alan R Liss, Inc., pp. 77-96 (1985).
	C24	Collins et al., "Continuous Growth and Differentiation of Human Myeloid Leukaemic Cells in Suspension-Culture," Nature, 270:347-349 (1977).
Examiner Signature		Date Considered

	PTO/SB/08a/b (08-03) Approved for use through 07/31/2006. OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.							
Substitute for form 1449A/B/PTO				Complete if Known				
				Application Number	10/774,802			
11	<b>IFORMATION</b>	1 DI	SCLOSURE	Filing Date	February 9, 2004			
S	TATEMENT E	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.			
				Art Unit	1646			
(Use as many sheets as necessary)			necessary)	Examiner Name	To be Assigned			
Sheet	4	of	18	Attorney Docket Number	28967/34891.1			

C25	De Gast, G.C. et al., "Clinical perspectives of bispecific antibodies in cancer," Cancer Immunol Immunother, 45:121-123 (1997).
C26	De Vries et al., "The fms-Like Tyrosine Kinase, a Receptor for Vascular Endothelial Growth Factor," Science, 255:989-991 (February 21, 1992).
C27	De Waal, R. et al., "Technical Advance: Lack of Lymphangiogenesis in Human Primary Cutaneous Melanoma," American Journal of Pathology, 150(6):1951-1957 (June, 1997).
C28	Devereux et al., "A Comprehensive Set of Sequence Analysis Programs for the VAX," Nucleic Acids Res., 12(1):387-395 (1984).
C29	Dias, et al., "Vascular endothelial growth factor (VEGF)-C signaling through FLt-4 (VEGFR-3) mediates leukemic cell proliferation, survival, and resistance to chemotherapy," Blood, 99:2179-2184 (2002)
C30	Dictor, M. et al., "Lymphaticovenous Differentiation in Kaposi's Sarcoma: Cellular Phenotypes by Stage," American Journal of Pathology, 130(2):411-417 (February, 1988).
C31	Edgell et al., "Permanent Cell Line Expressing Human Factor VIII-Related Antigen Established by Hybridization," Proc. Nat'l. Acad. Sci. USA, 50:3734-3737 (June, 1983).
C32	Eggert, A., et al., "High-Level Expression of Angiogenic Factors Is Associated with Advanced Tumor Stage in Human Neuroblastomas," Clin. Cancer Res., 6(5):1900-8 (May 2000).
C33	Eichmann <i>et al.</i> , "Molecular cloning of Quek 1 and 2, two quail vascular endothelial growth factor (VEGF) receptor-like molecules," <i>Gene, 174(1)</i> :3-8 (1996).
C34	Enholm, B. et al., "Vascular Endothelial Growth Factor-C, a Growth Factor for Lymphatic and Blood Vascular Endothelial Cells," TCM, 8(7):292-297 (1998).
C35	Fanger, M.W. et al., "Bispecific Antibodies," Critical Reviews in Immunology, 12(3,4):101-124 (1992).
C36	Ferrara, N. et al., "The Biology of Vascular Endothelial Growth Factor," Endocrine Reviews, 18(1):4-25 (1997).
C37	Fellmer, P.T., et al., "Vascular endothelial growth factor-C gene expression in papillary and follicular thyroid carcinomas," Surgery, 126(6):1056-61 (December 1999).

Examiner	Date	
Signature	Considered	

Sut	ostitute for form 1449A/B/PT	0		Complete if Known		
		_		Application Number	10/774,802	
11	NFORMATION	I DI	SCLOSURE	Filing Date	February 9, 2004	
l s	TATEMENT B	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
,	(Use as many sh	eets as	s necessary)	Examiner Name	To be Assigned	
Sheet	5	of	18	Attorney Docket Number	28967/34891.1	

	C38	Fielder W., et al., "Expression of FLT4 and its ligand VEGF-C in Acute Myeloid Leukemia," Leukemia, 8:1234-7 (August 1997) (Abstract).	
	C39	Finnerty et al., "Molecular Cloning g of Murine FLT and FLT4," Oncogene, 8(11):2293-2298 (1993).	
	C40	Flanagan & Leder, "The kit Ligand: A Cell Surface Molecule Altered in Steel Mutant Fibroblasts," Cell, 63:185-194 (October 5, 1990).	
	C41	Folkman et al., "Long-term culture of capillary endothelial cells," Proc. Nat'l Acad. Sci., USA, 76(10):5217-5221 (October, 1979).	
r.	C42	Folpe, A.L., et al., "Vascular Endothelial Growth Factor Receptor-3 (VEGFR-3): A Marker of Vascular Tumors with Presumed Lymphatic Differentiation, Including Kaposi's Sarcoma, Kaposiform and Dabska-Type Hemangioendotheliomas, and a Subset of Angiosarcomas," Mod. Pathol, 13(2):180-185 (2000).	
,	C43	Foote, J. et al., "Antibody Framework Residues Affecting the Conformation of the Hypervariable Loops," J. Mol. Biol., 224:487-499 (1992).	
	C44	Fortkamp et al., "Cloning and Expression in Escherichia coli of a Synthetic DNA for Hirudin, the Blood Coagulation Inhibitor in the Leech," DNA, 5(6):511-517 (1986).	
	C45	Fournier et al., "Mutation at Tyrosine Residue 1337 Abrogates Ligand-Dependent Transforming Capacity of the FLT4 Receptor," Oncogene, 11:921-931 (1995).	
	C46	Fournier et al., "Interaction with the Phosphotyrosine Binding Domain/Phosphotyrosine Interacting Domain of SHC Is Required for the Transforming Activity of the FLT4/VEGFR3 Receptor Tyrosine Kinase," J. Biological Chemistry, 271(22):12956-12963 (1996).	
	C47	Gahmberg et al., "Membrane Glycolysation During Cell Differentiation," In L. C. Andersson, et al. (ed.), Gene Expression During Normal and Malignant Differentiation, 107-123, Academic Press, London (1985).	
	C48	Galland et al., "Chromosomal Localization of FLT4, a Novel Receptor-Type Tyrosine Kinase Gene," Genomics, 13:475-478 (1992).	
	C49	Galland et al., "The FLT4 Gene Encodes a Transmembrane Tyrosine Kinase Related to the Vascular Endothelial Growth Factor Receptor," Oncogene, 8(11):1233-1240 (1993).	
	C50	Gasparini, G. et al., "Clinical Importance of the Determination of Tumor Angiogenesis in Breast Carcinoma: Much More Than a New Prognostic Tool," Journal of Clinical Oncology, 13(3):765-782 (March, 1995).	

Examiner	Date	
Signature	Considered	

Sub	stitute for form 1449A/B/	РТО		Complete if Known		
				Application Number	10/774,802	
II.	<b>IFORMATIO</b>	N DI	SCLOSURE	Filing Date	February 9, 2004	
S	<b>TATEMENT</b>	BY A	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
	(Use as many s	sheets as	necessary)	Examiner Name	To be Assigned	
Sheet	6	of	18	Attorney Docket Number	28967/34891.1	

Genbank Accession X51602 Human flt mRNA for receptor-related tyrosine kinase, deposited by Shibuya, M.
Genbank Accession X60280 plasmid pLTRpoly, deposited by Maekelae et al.
Genbank Accession X68203 H. sapiens mRNA for FLT4, Class III receptor tyrosine kinase, deposited by Aprelikova, O.
Genbank Accession X83287 C. coturnix Quek2 mRNA for vascular endothelial growth factor receptor, deposited by Eichmann, et al.
GenBank Accession No. AJ000185, Homo Sapiens mRNA for vascular endothelial growth factor-D, deposited by Achen, M.G.
Greenberg et al., "Characterization of a New Megakaryocyte Cell Line: The Dami Cell," Blood, 72(6):1968-1977 (December, 1988).
Gunningham, S.P., et al., "The Short Form of the Alternatively Spliced flt-4 but not Its Ligand Vascular Endothelial Growth Factor C Is Related to Lymph Node Metastasis in Human Breast Cancers," Clin. Cancer Res., 6(11):4278-86 (November 2000).
Harlow et al., Antibodies: A Laboratory Manual, pp.72-137, 141-157, 287 & 321-358 (1988).
Hatva et al., "Expression of Endothelial Cell-Specific Receptor Tyrosine Kinases and Growth Factors in Human Brain Tumors," Am. J. Pathol., 146:368-378 (1995).
Hatva, E., et al., "Vascular Growth Factors and Receptors in Capillary Hemangioblastomas and Hemangiopericytomas," Am. J. Pathol, 148(3):763-75 (March 1996).
Heldin et al., "Platelet-Derived Growth Factor: Mechanism of Action and Possible in Vivo Function," Cell Regulation, 1:555-566 (July, 1990).
Hemmila et al., "Europium as a Label in Time-Resolved Immunofluorometric Assays," Annal. Biochem, 137:335-343 (1984).
Hewett, P.W. et al., "Coexpression of flt-1, flt-4 and KDR in Freshly Isolated and Cultured Human Endothelial Cells," Biochemical and Biophysical Research Communications, 221:697-702 (1996).
Hirai et al., "A Novel Putative Tyrosine Kinase Receptor Encoded by the eph Gene," Science, 238:1717-1720 (1987).
Hoogenboom, H.R., "Designing and optimizing library selection strategies for generating high-affinity antibodies," TIBTECH, 15:62-70-(1997).
Date Considered

	PTO/SB/08a/b (08-03) Approved for use through 07/31/2006. OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.						
Sub	stitute for form 1449A/B/PT	o .	***		Complete if Known		
		_		Application Number	10/774,802		
11	<b>IFORMATION</b>	I DI	SCLOSURE	Filing Date	February 9, 2004		
S	TATEMENT B	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.		
				Art Unit	1646		
	(Use as many she	eets as	necessary)	Examiner Name	To be Assigned		
Sheet	7	of	18	Attorney Docket Number	28967/34891.1		

C66	 							
Huang et al., "The Hematopoietic Growth Factor KL is Encoded by the SI Locus and is the Ligand of the c-kit Receptor, the Gene Product of the W Locus," Cell, 63:225-33 (October 5, 1990).  C68  Hunter & Greenwood, "Preparation of Iodine-131 Labelled Human Growth Hormone of High Specific Activity," Nature, 194(4827):495-496 (May 5, 1962).  C69  Jacquemier, J., et al., "Prognosis of Breast-Carcinoma Lymphagenesis Evaluated by Immunohistochemical Investigation of Vascular-Endothelial-Growth-Factor Receptor 3," Int. J. Cancer (Pred. Oncol.), 89:69-73 (2000).  C70  Jeltsch, "Hyperplasia of Lymphatic Vessels in VEGF-C Transgenic Mice," Science, 276:1423-1425 (May 30, 1997).  C71  Jones, P.T. et al., "Replacing the complementarity-determining regions in a human antibody with those from a mouse," Nature, 321:522-525 (May, 1986).  C72  Jones, A., et al., "Angiogenesis and lymphangiogenesis in stage 1 germ cell tumours of the testis," BJU International, 86:80-86 (2000).  C73  Joukov, V. et al., "Proteolytic processing regulates receptor specificity and activity of VEGF-C," EMBO Journal, 16(13):3398-3911 (June, 1997).  C74  Joukov et al., "A Novel Vascular Endothelial Growth Factor, VEGF-C, is a Ligand for the Flt4 (VEGFR-3) and KDR (VEGFR-2) Receptor Tyrosine Kinases," EMBO J., 15(2):290-298 (January 15, 1996).  C75  Jussila, L. et al., "Lymphatic Endothelium and Kaposi's Sarcoma Spindle Cells Detected by Antibodies against the Vascular Endothelial Growth Factor Receptor-3," Cancer Res., 58:1599-1604 (April, 1998).  Kaipainen et al., "Expression of the FMS-Like Tyrosine Kinase 4 Gene Becomes Restricted to Lymphatic Endothelium During Development," Proc. Nat'l Acad. Sci., USA, 92:3566-3570 (April, 1995).  Kaipainen et al., "The Related FLT4, FLT1, and KDR Receptor Tyrosine Kinases Show Distinct Expression Patterns in Human Fetal Endothelial Cells," J. Exp. Med., 178:2077-2088 (December, 1993).  C78  Karkkainen, M.J., et al., "Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenes	C66	VEGF-2 for Vascular Endothelial and Smooth Muscle Cells," The FASEB Journal,						
Hunter & Greenwood, "Preparation of Iodine-131 Labelled Human Growth Hormone of High Specific Activity," Nature, 194(4827):495-496 (May 5, 1962).  C69  Jacquemier, J., et al., "Prognosis of Breast-Carcinoma Lymphagenesis Evaluated by Immunohistochemical Investigation of Vascular-Endothelial-Growth-Factor Receptor 3," Int. J. Cancer (Pred. Oncol.), 89:69-73 (2000).  C70  Jeltsch, "Hyperplasia of Lymphatic Vessels in VEGF-C Transgenic Mice," Science, 276:1423-1425 (May 30, 1997).  C71  Jones, P.T. et al., "Replacing the complementarity-determining regions in a human antibody with those from a mouse," Nature, 321:522-525 (May, 1986).  C72  Jones, A., et al., "Angiogenesis and lymphangiogenesis in stage 1 germ cell tumours of the testis," BJU International, 86:80-86 (2000).  C73  Joukov, V. et al., "Proteolytic processing regulates receptor specificity and activity of VEGF-C," EMBO Journal, 16(13):3898-3911 (June, 1997).  C74  Joukov et al., "A Novel Vascular Endothelial Growth Factor, VEGF-C, is a Ligand for the Flt4 (VEGFR-3) and KDR (VEGFR-2) Receptor Tyrosine Kinases," EMBO J., 15(2):290-298 (January 15, 1996).  C75  Jussila, L. et al., "Lymphatic Endothelium and Kaposi's Sarcoma Spindle Cells Detected by Antibodies against the Vascular Endothelial Growth Factor Receptor-3," Cancer Res., 58:1599-1604 (April, 1998).  C76  Kaipainen et al., "Expression of the FMS-Like Tyrosine Kinase 4 Gene Becomes Restricted to Lymphatic Endothelium During Development," Proc. Nat'l Acad. Sci., USA, 92:3566-3570 (April, 1995).  C77  Kaipainen et al., "The Related FLT4, FLT1, and KDR Receptor Tyrosine Kinases Show Distinct Expression Patterns in Human Fetal Endothelial Cells," J. Exp. Med., 178:2077-2088 (December, 1993).  Karkkainen, M.J., et al., "Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenesis," Oncogene, 19(49):5598-605 (November 20, 2000).	C67	is the Ligand of the c-kit Receptor, the Gene Product of the W Locus," Cell, 63:225-						
Jacquemier, J., et al., "Prognosis of Breast-Carcinoma Lymphagenesis Evaluated by Immunohistochemical Investigation of Vascular-Endothelial-Growth-Factor Receptor 3," Int. J. Cancer (Pred. Oncol.), 89:69-73 (2000).  C70  Jeltsch, "Hyperplasia of Lymphatic Vessels in VEGF-C Transgenic Mice," Science, 276:1423-1425 (May 30, 1997).  C71  Jones, P.T. et al., "Replacing the complementarity-determining regions in a human antibody with those from a mouse," Nature, 321:522-525 (May, 1986).  C72  Jones, A., et al., "Angiogenesis and lymphangiogenesis in stage 1 germ cell tumours of the testis," BJU International, 86:80-86 (2000).  C73  Joukov, V. et al., "Proteolytic processing regulates receptor specificity and activity of VEGF-C," EMBO Journal, 16(13):3898-3911 (June, 1997).  C74  Joukov et al., "A Novel Vascular Endothelial Growth Factor, VEGF-C, is a Ligand for the Flt4 (VEGFR-3) and KDR (VEGFR-2) Receptor Tyrosine Kinases," EMBO J., 15(2):290-298 (January 15, 1996).  C75  Jussila, L. et al., "Lymphatic Endothelium and Kaposi's Sarcoma Spindle Cells Detected by Antibodies against the Vascular Endothelial Growth Factor Receptor-3," Cancer Res., 58:1599-1604 (April, 1998).  C76  Kaipainen et al., "Expression of the FMS-Like Tyrosine Kinase 4 Gene Becomes Restricted to Lymphatic Endothelium During Development," Proc. Nat'l Acad. Sci., USA, 92:3566-3570 (April, 1995).  C77  Kaipainen et al., "The Related FLT4, FLT1, and KDR Receptor Tyrosine Kinases Show Distinct Expression Patterns in Human Fetal Endothelial Cells," J. Exp. Med., 178:2077-2088 (December, 1993).  C78  Karkkainen, M.J., et al., "Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenesis," Oncogene, 19(49):5598-605 (November 20; 2000).	C68							
Jeltsch, "Hyperplasia of Lymphatic Vessels in VEGF-C Transgenic Mice," Science, 276:1423-1425 (May 30, 1997).    C71	C69.	Immunohistochemical Investigation of Vascular-Endothelial-Growth-Factor						
C71 Jones, P.T. et al., "Replacing the complementarity-determining regions in a human antibody with those from a mouse," Nature, 321:522-525 (May, 1986).  C72 Jones, A., et al., "Angiogenesis and lymphangiogenesis in stage 1 germ cell tumours of the testis," BJU International, 86:80-86 (2000).  C73 Joukov, V. et al., "Proteolytic processing regulates receptor specificity and activity of VEGF-C," EMBO Journal, 16(13):3898-3911 (June, 1997).  C74 Joukov et al., "A Novel Vascular Endothelial Growth Factor, VEGF-C, is a Ligand for the FIt4 (VEGFR-3) and KDR (VEGFR-2) Receptor Tyrosine Kinases," EMBO J., 15(2):290-298 (January 15, 1996).  C75 Jussila, L. et al., "Lymphatic Endothelium and Kaposi's Sarcoma Spindle Cells Detected by Antibodies against the Vascular Endothelial Growth Factor Receptor-3," Cancer Res., 58:1599-1604 (April, 1998).  C76 Kaipainen et al., "Expression of the FMS-Like Tyrosine Kinase 4 Gene Becomes Restricted to Lymphatic Endothelium During Development," Proc. Nat'l Acad. Sci., USA, 92:3566-3570 (April, 1995).  C77 Kaipainen et al., "The Related FLT4, FLT1, and KDR Receptor Tyrosine Kinases Show Distinct Expression Patterns in Human Fetal Endothelial Cells," J. Exp. Med., 178:2077-2088 (December, 1993).  C78 Karkkainen, M.J., et al., "Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenesis," Oncogene, 19(49):5598-605 (November 20, 2000).	C70							
Jones, A., et al., "Angiogenesis and lymphangiogenesis in stage 1 germ cell tumours of the testis," BJU International, 86:80-86 (2000).  C73  Joukov, V. et al., "Proteolytic processing regulates receptor specificity and activity of VEGF-C," EMBO Journal, 16(13):3898-3911 (June, 1997).  C74  Joukov et al., "A Novel Vascular Endothelial Growth Factor, VEGF-C, is a Ligand for the Flt4 (VEGFR-3) and KDR (VEGFR-2) Receptor Tyrosine Kinases," EMBO J., 15(2):290-298 (January 15, 1996).  C75  Jussila, L. et al., "Lymphatic Endothelium and Kaposi's Sarcoma Spindle Cells Detected by Antibodies against the Vascular Endothelial Growth Factor Receptor-3," Cancer Res., 58:1599-1604 (April, 1998).  C76  Kaipainen et al., "Expression of the FMS-Like Tyrosine Kinase 4 Gene Becomes Restricted to Lymphatic Endothelium During Development," Proc. Nat'l Acad. Sci., USA, 92:3566-3570 (April, 1995).  C77  Kaipainen et al., "The Related FLT4, FLT1, and KDR Receptor Tyrosine Kinases Show Distinct Expression Patterns in Human Fetal Endothelial Cells," J. Exp. Med., 178:2077-2088 (December, 1993).  C78  Karkkainen, M.J., et al., "Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenesis," Oncogene, 19(49):5598-605 (November 20, 2000).	C71							
Joukov, V. et al., "Proteolytic processing regulates receptor specificity and activity of VEGF-C," EMBO Journal, 16(13):3898-3911 (June, 1997).  C74  Joukov et al., "A Novel Vascular Endothelial Growth Factor, VEGF-C, is a Ligand for the Flt4 (VEGFR-3) and KDR (VEGFR-2) Receptor Tyrosine Kinases," EMBO J., 15(2):290-298 (January 15, 1996).  C75  Jussila, L. et al., "Lymphatic Endothelium and Kaposi's Sarcoma Spindle Cells Detected by Antibodies against the Vascular Endothelial Growth Factor Receptor-3," Cancer Res., 58:1599-1604 (April, 1998).  C76  Kaipainen et al., "Expression of the FMS-Like Tyrosine Kinase 4 Gene Becomes Restricted to Lymphatic Endothelium During Development," Proc. Nat'l Acad. Sci., USA, 92:3566-3570 (April, 1995).  C77  Kaipainen et al., "The Related FLT4, FLT1, and KDR Receptor Tyrosine Kinases Show Distinct Expression Patterns in Human Fetal Endothelial Cells," J. Exp. Med., 178:2077-2088 (December, 1993).  C78  Karkkainen, M.J., et al., "Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenesis," Oncogene, 19(49):5598-605 (November 20, 2000).	C72							
Joukov et al., "A Novel Vascular Endothelial Growth Factor, VEGF-C, is a Ligand for the Flt4 (VEGFR-3) and KDR (VEGFR-2) Receptor Tyrosine Kinases," EMBO J., 15(2):290-298 (January 15, 1996).  C75  Jussila, L. et al., "Lymphatic Endothelium and Kaposi's Sarcoma Spindle Cells Detected by Antibodies against the Vascular Endothelial Growth Factor Receptor-3," Cancer Res., 58:1599-1604 (April, 1998).  C76  Kaipainen et al., "Expression of the FMS-Like Tyrosine Kinase 4 Gene Becomes Restricted to Lymphatic Endothelium During Development," Proc. Nat'l Acad. Sci., USA, 92:3566-3570 (April, 1995).  C77  Kaipainen et al., "The Related FLT4, FLT1, and KDR Receptor Tyrosine Kinases Show Distinct Expression Patterns in Human Fetal Endothelial Cells," J. Exp. Med., 178:2077-2088 (December, 1993).  C78  Karkkainen, M.J., et al., "Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenesis," Oncogene, 19(49):5598-605 (November 20, 2000).	C73							
Jussila, L. et al., "Lymphatic Endothelium and Kaposi's Sarcoma Spindle Cells Detected by Antibodies against the Vascular Endothelial Growth Factor Receptor-3," Cancer Res., 58:1599-1604 (April, 1998).  C76  Kaipainen et al., "Expression of the FMS-Like Tyrosine Kinase 4 Gene Becomes Restricted to Lymphatic Endothelium During Development," Proc. Nat'l Acad. Sci., USA, 92:3566-3570 (April, 1995).  C77  Kaipainen et al., "The Related FLT4, FLT1, and KDR Receptor Tyrosine Kinases Show Distinct Expression Patterns in Human Fetal Endothelial Cells," J. Exp. Med., 178:2077-2088 (December, 1993).  C78  Karkkainen, M.J., et al., "Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenesis," Oncogene, 19(49):5598-605 (November 20, 2000).	C74	for the Flt4 (VEGFR-3) and KDR (VEGFR-2) Receptor Tyrosine Kinases," EMBO						
Kaipainen et al., "Expression of the FMS-Like Tyrosine Kinase 4 Gene Becomes Restricted to Lymphatic Endothelium During Development," Proc. Nat'l Acad. Sci., USA, 92:3566-3570 (April, 1995).    C77	C75	Jussila, L. et al., "Lymphatic Endothelium and Kaposi's Sarcoma Spindle Cells Detected by Antibodies against the Vascular Endothelial Growth Factor Receptor-3,"						
Kaipainen et al., "The Related FLT4, FLT1, and KDR Receptor Tyrosine Kinases   Show Distinct Expression Patterns in Human Fetal Endothelial Cells," J. Exp. Med., 178:2077-2088 (December, 1993).    C78	C76	Restricted to Lymphatic Endothelium During Development," Proc. Nat'l Acad. Sci.,						
Karkkainen, M.J., et al., "Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenesis," Oncogene, 19(49):5598-605 (November 20, 2000).  Examiner Date	C77	Kaipainen et al., "The Related FLT4, FLT1, and KDR Receptor Tyrosine Kinases Show Distinct Expression Patterns in Human Fetal Endothelial Cells," J. Exp. Med.,						
	C78	regulation of angiogenesis and lymphangiogenesis," Oncogene, 19(49):5598-605						

	Under the Paperwork	Reducti	on Act of 1995, no persons are rec	U.S. Patent and Tra	PTO/SB/08a/b (08-03) oproved for use through 07/31/2006. OMB 0651-0031 idemark Office; U.S. DEPARTMENT OF COMMERCE finformation unless it contains a valid OMB control number.
Sub	stitute for form 1449A/B/PT	0			Complete if Known
		_		Application Number	10/774,802
11	<b>IFORMATION</b>	I DI	SCLOSURE	Filing Date	February 9, 2004
S	TATEMENT E	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.
				Art Unit	1646
	(Use as many sh	eets as	necessary)	Examiner Name	To be Assigned
Sheet 8 of 18				Attorney Docket Number	28967/34891.1

	C79	Karkkainen, et al., "Lymphatic endothelium: a new frontier of metastasis research,"  Nat. Cell. Biol. 4:E2-E5 (2002)
	C80	Karpanen, et al., "Vascular endothelial growth factor C promotes tumor lymphangiogenesis and intralymphatic tumor growth," Cancer Res. 61:1786-90 (2001)
	C81	Kerstens, H. et al., "A Novel In Situ Hybridization Signal Amplification Method Based on the Deposition of Biotinylated Tyramine," Journal Histochemistry and Cytochemistry, 43(4):347-352 (1995).
	C82	Kettleborough, C.A. <i>et al.</i> , "Humanization of a mouse monoclonal antibody by CDR-grafting: the importance of framework residues on loop conformation," Protein Engineering, 4(7):773-783 (1991).
	C83	Kieffer et al., "Uncoupling in the Expression of Platelet GP IIb/IIIa in Human Endothelial Cells and K562 Cells: Absence of Immunologic Crossreactivity Between Platelet GP IIb and the Vitronectin Receptor Alpha Chain," Blood, 72(4):1209-1215 (October, 1988).
-	C84	Kim, K.J. et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumour growth in vivo," Nature, 362(6423):841-844 (April, 1993).
	C85	Koeffler et al., "Acute Myelogenous Leukemia: A Human Cell Line Responsive to Colony-Stimulating Activity," Science, 200:1153-1154 (1978).
	C86	Köhler et al., "Continuous Cultures of Fused Cells Secreting Antibody of Predefined Specificity," Nature, 256:495-497 (August 7, 1975).
	C87	Korhonen <i>et al.</i> , "Enhanced Expression of the <i>tie</i> Receptor Tyrosine Kinase in Endothelial Cells During Neovascularization," <i>Blood</i> , <i>80(10)</i> :2548-2555 (November 15, 1992).
	C88	Korhonen et al., "The Mouse Tie Receptor Tyrosine Kinase Gene: Expression During Embryonic Angiogenesis," Oncogene (England), 9(2):395-403 (February, 1994).
	C89	Kozbor et al., "The Production of Monoclonal Antibodies From Human Lymphocytes," Immunology Today, 4(3):72-79 (1983).
	C90	Kubo, H., et al., "Involvement of vascular endothelial growth factor receptor-3 in maintenance of integrity of endothelial cell lining during tumor angiogenesis," Blood, 96(2):546-553 (15 July 2000).

IExaminer I IDate I	
Signature Considered	

Sub	stitute for form 1449A/B/PT	0		Complete if Known		
		•		Application Number	10/774,802	
II.	<b>IFORMATION</b>	I DI	SCLOSURE	Filing Date	February 9, 2004	
S	TATEMENT B	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
	(Use as many sh	eets as	necessary)	Examiner Name	To be Assigned	
Sheet	9	of	18	Attorney Docket Number	28967/34891.1	

C91	Kukk et al., "VEGF-C Receptor Binding and Pattern of Expression with VEGFR-3 Suggests A Role in Lymphatic Vascular Development," <i>Development</i> , 122:3829-3837 (December, 1996).	
C92	Kurebayashi, J., et al., "Expression of Vascular Endothelial Growth Factor (VEGF) Family Members in Breast Cancer," <i>Jpn. J. Cancer Res., 90(9)</i> :977-81 (September 1999).	
C93	Lee et al., "Vascular Endothelial Growth Factor-Related Protein: A Ligand and Specific Activator of the Tyrosine Kinase Receptor Flt4," Proc. Natl. Acad. Sci., USA, 93:1988-1992 (March, 1996).	
C94	Leu, et al., "Absence of functional lymphatics within a murine sarcoma: a molecular and functional evaluation," Cancer Res. 60:4324-7 (2000)	
C95	Lhotak et al., "Characterization of Elk, a Brain-Specific Receptor Tyrosine Kinase," Mol. Cell. Biol., 11:2496-2502 (May, 1991).	
C96	Lindberg et al. "cDNA Cloning and Characterization of eck, an Epithelial Cell Receptor Protein-Tyrosine Kinase in the eph/elk Family of Protein Kinases," Mol. Cell. Biol., 10:6316-6324 (December, 1990).	
C97	Lovgren et al., "Time-Resolved Fluorometry in Immunoassay," In: Collins W.P. (Ed.) Alternative Immunoassays, John Wiley & Sons Ltd., pp.203-217 (1985).	
C98	Lozzio et al., "Human Chronic Myelogenous Leukemia Cell-Line With Positive Philadelphia Chromosome," Blood, 45(3):321-334 (March, 1975).	
C99	Lyman <i>et al.</i> , "Molecular Cloning of a Ligand for the flt3/flk-2 Tyrosine Kinase Receptor: A Proliferative Factor for Primitive Hematopoietic Cells," <i>Cell</i> , 75:1157-1167 (December 17, 1993).	
C100	Lymboussaki, A. et al., "Expression of the Vascular Endothelial Growth Factor C Receptor VEGFR-3 in Lymphatic Endothelium of the Skin and in Vascular Tumors," American Journal of Pathology, 153(2):395-403 (August, 1998).	
C101	Makela et al., "Plasmid pLTRpoly: a Versatile High-Efficiency Mammalian Expression Vector," Gene, 118:293-294 (1992).	
C102	Makinen, et al., "Inhibition of lymphangiogenesis with resulting lymphedema in transgenic mice expressing soluble VEGF receptor-3," Nat. Med. 7:199-205 (2001)	
C103	Marchio, S., et al., "Vascular Endothelial Growth Factor-C Stimulates the Migration and Proliferation of Kaposi's Sarcoma Cells," J. Biol. Chem., 274(39):27617-22 (September 24, 1999).	

	Date		Examiner
	Considered		Signature
	Considered		Signature

PTO/SB/08a/b (08-03) Approved for use through 07/31/2006. OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.							
Substitute for form 1449A/B/PTO Complete if Known							
Cabballate for form 144070B/110				Application Number	10/774,802		
IN	<b>IFORMATION</b>	l Di	SCLOSURE	Filing Date	February 9, 2004		
STATEMENT BY APPLICANT				First Named Inventor	Kari Alitalo et al.		
					1646		
(Use as many sheets as necessary)				Examiner Name	To be Assigned		
Sheet	10	of	18	Attorney Docket Number	28967/34891.1		

C104 Marconcini, L., et al., "c-fos-induced growth factor/vascular endothelial growth factor D induces angiogenesis in vivo and in vitro," Proc. Natl. Acad. Sci. USA, 96:9671-76 (August 1999).  C105 Martin et al., "HEL Cells: A New Human Erythroleukemia Cell Line With Spontaneous Induced Globin Expression," Science, 216:1233-1235 (1982).  C106 Matthews et al., "A Receptor Tyrosine Kinase cDNA Isolated From a Population of Enriched Primitive Hematopoietic Cells and Exhibiting Close Genetic Linkage to c-kit," Proc. Natl. Acad. Sci. USA, 88(20):9026-9030 (October, 1991).  C107 Matthews et al., "A Receptor Tyrosine Kinase Specific to Hematopoietic Stem and Progenitor Cell-Enriched Populations," Cell, 65(7):1143-1152 (June 28, 1991).  C108 Mattila, et al., "VEGF-C induced lymphangiogenesis is associated with lymph node metastasis in orthotopic MCF-7 tumors," Int. J. Cancer. 98:946-951 (2002)  C109 McCutchan et al., "Enhancement of the Infectivity of Simian Virus 40 Deoxyribonucleic Acid with Diethylaminoethyl-Dectran," J. Natl. Cancer Inst., 41:351-357 (1968).  C110 Mikayama T., Molecular Cloning and Functional Expression of a cDNA Encoding Glycosylation-Inhibiting Factor. Proc. Natl. Acad. Sci. USA Vol. 90, pages 10056-10060, 1993.  C112	
Martin et al., "HEL Cells: A New Human Erythroleukemia Cell Line With Spontaneous Induced Globin Expression," Science, 216:1233-1235 (1982).  C106  Matthews et al., "A Receptor Tyrosine Kinase cDNA Isolated From a Population of Enriched Primitive Hematopoietic Cells and Exhibiting Close Genetic Linkage to c-kit," Proc. Natl. Acad. Sci. USA, 88(20):9026-9030 (October, 1991).  C107  Matthews et al., "A Receptor Tyrosine Kinase Specific to Hematopoietic Stem and Progenitor Cell-Enriched Populations," Cell, 65(7):1143-1152 (June 28, 1991).  C108  Mattila, et al., "VEGF-C induced lymphangiogenesis is associated with lymph node metastasis in orthotopic MCF-7 tumors," Int. J. Cancer. 98:946-951 (2002)  C109  McCutchan et al., "Enhancement of the Infectivity of Simian Virus 40 Deoxyribonucleic Acid with Diethylaminoethyl-Dectran," J. Natl. Cancer Inst., 41:351-357 (1968).  C110  Metzelaar et al., "CD63 Antigen," J. Biol. Chem., 266(5):3239-3245 (February 15, 1991).  C111  Mikayama T., Molecular Cloning and Functional Expression of a cDNA Encoding Glycosylation-Inhibiting Factor. Proc. Natl. Acad. Sci. USA Vol. 90, pages 10056-10060, 1993.	
Matthews et al., "A Receptor Tyrosine Kinase cDNA Isolated From a Population of Enriched Primitive Hematopoietic Cells and Exhibiting Close Genetic Linkage to c-kit," Proc. Natl. Acad. Sci. USA, 88(20):9026-9030 (October, 1991).  C107  Matthews et al., "A Receptor Tyrosine Kinase Specific to Hematopoietic Stem and Progenitor Cell-Enriched Populations," Cell, 65(7):1143-1152 (June 28, 1991).  C108  Mattila, et al., "VEGF-C induced lymphangiogenesis is associated with lymph node metastasis in orthotopic MCF-7 tumors," Int. J. Cancer. 98:946-951 (2002)  C109  McCutchan et al., "Enhancement of the Infectivity of Simian Virus 40 Deoxyribonucleic Acid with Diethylaminoethyl-Dectran," J. Natl. Cancer Inst., 41:351-357 (1968).  C110  Metzelaar et al., "CD63 Antigen," J. Biol. Chem., 266(5):3239-3245 (February 15, 1991).  C111  Mikayama T., Molecular Cloning and Functional Expression of a cDNA Encoding Glycosylation-Inhibiting Factor. Proc. Natl. Acad. Sci. USA Vol. 90, pages 10056-10060, 1993.	
Matthews.et al., "A Receptor Tyrosine Kinase Specific to Hematopoietic Stem and Progenitor Cell-Enriched Populations," Cell, 65(7):1143-1152 (June 28, 1991).  C108  Mattila, et al., "VEGF-C induced lymphangiogenesis is associated with lymph node metastasis in orthotopic MCF-7 tumors," Int. J. Cancer. 98:946-951 (2002)  C109  McCutchan et al., "Enhancement of the Infectivity of Simian Virus 40 Deoxyribonucleic Acid with Diethylaminoethyl-Dectran," J. Natl. Cancer Inst., 41:351-357 (1968).  C110  Metzelaar et al., "CD63 Antigen," J. Biol. Chem., 266(5):3239-3245 (February 15, 1991).  C111  Mikayama T., Molecular Cloning and Functional Expression of a cDNA Encoding Glycosylation-Inhibiting Factor. Proc. Natl. Acad. Sci. USA Vol. 90, pages 10056-10060, 1993.	
Mattila, et al., "VEGF-C induced lymphangiogenesis is associated with lymph node metastasis in orthotopic MCF-7 tumors," Int. J. Cancer. 98:946-951 (2002)  C109  McCutchan et al., "Enhancement of the Infectivity of Simian Virus 40 Deoxyribonucleic Acid with Diethylaminoethyl-Dectran," J. Natl. Cancer Inst., 41:351-357 (1968).  C110  Metzelaar et al., "CD63 Antigen," J. Biol. Chem., 266(5):3239-3245 (February 15, 1991).  C111  Mikayama T., Molecular Cloning and Functional Expression of a cDNA Encoding Glycosylation-Inhibiting Factor. Proc. Natl. Acad. Sci. USA Vol. 90, pages 10056-10060, 1993.	
McCutchan et al., "Enhancement of the Infectivity of Simian Virus 40 Deoxyribonucleic Acid with Diethylaminoethyl-Dectran," J. Natl. Cancer Inst., 41:351-357 (1968).  C110  Metzelaar et al., "CD63 Antigen," J. Biol. Chem., 266(5):3239-3245 (February 15, 1991).  C111  Mikayama T., Molecular Cloning and Functional Expression of a cDNA Encoding Glycosylation-Inhibiting Factor. Proc. Natl. Acad. Sci. USA Vol. 90, pages 10056- 10060, 1993.	
<ul> <li>Metzelaar et al., "CD63 Antigen," J. Biol. Chem., 266(5):3239-3245 (February 15, 1991).</li> <li>Mikayama T., Molecular Cloning and Functional Expression of a cDNA Encoding Glycosylation-Inhibiting Factor. Proc. Natl. Acad. Sci. USA Vol. 90, pages 10056-10060, 1993.</li> </ul>	
Mikayama T., Molecular Cloning and Functional Expression of a cDNA Encoding Glycosylation-Inhibiting Factor. Proc. Natl. Acad. Sci. USA Vol. 90, pages 10056-10060, 1993.	
Millauer et al., "High Affinity VEGF Binding and Developmental Expression Suggest Flk-1 as a Major Regulator of Vasculogenesis and Angiogenesis, Cell, 72:835-846 (March 26, 1993).	,
Minowada et al., "Brief Communication: Rosette-Forming Human Lymphoid Cell Lines: Establishment and Evidence for Origin of Thymus-Derived Lymphocytes," J. Natl. Cancer Inst., 49:891-895 (1972).	
Mollinedo et al., "Early and Selective Induction of Apoptosis in Human Leukemic Cells By the Alkyl-Lysophospholipid ET-18-OCH <sub>3</sub> ," Biochem. & Biophys. Res. Comm., 192(2):603-609 (April 30, 1993).	
Moriyama, M., et al., "Immunohistochemical Study of Tumour Angiogenesis in Oral Squamous Cell Carcinoma," Oral Oncol., 33(5):369-74 (September 1997).	
Moroni et al., "EGF-R Antisense RNA Blocks Expression of the Epidermal Growth Factor Receptor and Suppresses the Transforming Phenotype of a Human Carcinoma Cell Line," JBiol. Chem., 267(5):2714-2722 (February 5, 1992).	
Examiner Date Signature Considered	

Sub	stitute for form 1449A/B/PT	0		Complete if Known		
		_		Application Number	10/774,802	
11	<b>IFORMATION</b>	1 DI	SCLOSURE	Filing Date	February 9, 2004	
S	TATEMENT I	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
(Use as many sheets as necessary)				Examiner Name	To be Assigned	
Sheet	11	of	18	Attorney Docket Number 28967/34891.1		

C117	Morrison, S.L. et al., "Genetically Engineered Antibody Molecules," Advances in Immunology, 44:65-92 (1989).
C118	Moshakis, V. et al., "Localization of human breast-carcinoma xenografts using antibodies to carcinoembryonic antigen," Br. J. Cancer, 43:575-581 (1981).
C119	Mukkala et al., "The Synthesis and Use of Activated N-Benzyl Derivatives of Diethylenetriaminetetraacetic Acids: Alternative Reagents for Labeling of Antibodies with Metal Ions," Annal. Biochem, 176:319-325 (1989).
C120	Mustonen et al., "Endothelial Receptor Tyrosine Kinases Involved in Angiogenesis,"  J. Cell Biology, 129(4):895-898 (1995).
C121	Nathanson, S.D., et al., "Microvessels That Predict Axillary Lymph Node Metastases in Patients With Breast Cancer," Arch Surg, 135(5):586-93 (May 2000).
C122	Nicosia, R.F., "What Is the Role of Vascular Endothelial Growth Factor-Related Molecules in Tumor Angiogenesis?" Am. J. Pathol, 153(1):11-6 (July 1998).
C123	Niki, T., et al., "Expression of Vascular Endothelial Growth Factors A, B, C, and D and Their Relationships to Lymph Node Status in Lung Adenocarcinoma," Clin. Cancer Res., 6(6):2431-9 (June 2000).
C124	Nowell <i>et al.</i> , "Chromosome Studies in Preleukemic States: Myeloproliferative versus Cytopenic Disorders," <i>Cancer</i> , 42:2254-2260 (1978).
C125	Oelrichs et al., "NYK/FLK-1: A Putative Receptor Protein Tyrosine Kinase Isolated From E10 Embryonic Neuroepithelium is Expressed in Endothelial Cells of the Developing Embryo," Oncogene, 8(1):11-18 (January, 1993).
C126	Ohta, Y., et al., "Increased Vascular Endothelial Growth Factor and Vascular Endothelial Growth Factor-C and Decreased NM23 Expression Associated with Microdissemination in the Lymph Nodes in Stage 1 Non-Small Cell Lung Cancer,"  J. Thorac Cardiovasc Surg, 119(4 Pt 1):804-13 (April 2000).
C127	Ohta, Y., et al., "VEGF and VEGF type C play an important role in angiogenesis and lymphangiogenesis in human malignant mesothelioma tumours," Br. J. Cancer, 81(1):54-61 (September 1999).
C128	O'Reilly, M.S. <i>et al.</i> , "Angiostatin: A Novel Angiogenesis Inhibitor That Mediates the Suppression of Metastases by a Lewis Lung Carcinoma," <i>Cell</i> , 79(2):315-328 (October, 1994).
C129	O'Reilly, M.S. et al., "Endostatin: An Endogenous Inhibitor of Angiogenesis and Tumor Growth," Cell, 88(2):277-285 (January, 1997).

Examiner	Date	
Signature	 Considered	

Sub	stitute for form 1449A/B/PT	0		Complete if Known		
000		•		Application Number	10/774,802	
IN	<b>IFORMATION</b>	1 DI	SCLOSURE	Filing Date	February 9, 2004	
S	TATEMENT I	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
(Use as many sheets as necessary)			necessary)	Examiner Name	To be Assigned	
Sheet	12	of	18	Attorney Docket Number	28967/34891.1	

10400	
C130	Oh et al., "VEGF and VEGF-C: Specific Induction of Angiogenesis and Lymphangiogenesis in the Differentiated Avian Chorioallantoic Membrane," Developmental Biology, 188:96-109 (1997).
C131	Padlan, E.A., "A Possible Procedure For Reducing The Immunogenicity Of Antibody Variable Domains While Preserving Their Ligand-Binding Properties," <i>Molecular Immunology, 28(4/5)</i> :489-498 (1991).
C132	Pajusola et al., "FLT4 Receptor Tyrosine Kinase Contains Seven Immunoglobulin- Like Loops and is Expressed in Multiple Human Tissues and Cell Lines," <i>Cancer Research</i> , 52(20):5738-5743 (October 15, 1992).
C133	Pajusola et al., "Two Human FLT4 Receptor Tyrosine Kinase Isoforms With Distinct Carboxy Terminal Tails are Produced by Alternative Processing of Primary Transcripts," Oncogene, 8:2931-2937 (1993).
C134	Pajusola, "Cloning and Characterization of a New Endothelial Receptor Tyrosine Kinase FLT4 and Two Novel VEGF-Like Growth Factors VEGF-B and VEGF-C," Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute and Department of Biosciences, Division of Genetics, University of Helsinki, Academic Dissertation, Helsinki 1996.
C135	Pajusola et al., "Signalling Properties of FLT4, a Proteolytically Processed Receptor Tyrosine Kinase Related To Two VEGF Receptors," Oncogene, 9:3545-3555 (1994).
C136	Partanen et al., "A Novel Endothelial Cell Surface Receptor Tyrosine Kinase with Extracellular Epidermal Growth Factor Homology Domains," Mol. Cell. Biol., 12(4):1698-1707 (April, 1992).
C137	Partanen et al., "Putative Tyrosine Kinases Expressed in K-562 Human Leukemia Cells," Proc. Nat'l Acad. Sci., USA, 87(22):8913-8917 (November, 1990).
C138	Partanen, T.A., et al., "Lack of Lymphatic Vascular Specificity of Vascular Endothelial Growth Factor Receptor 3 in 185 Vascular Tumors," Cancer, 86(11):406-12 (December 1, 1999).
C139	Patent Cooperation Treaty Search Report for PCT/US 99/23525
C140	Perumov et al., "Influence of Antisense RNA's of Interleukin-1β and Interleukin-1 Receptor Antagonist on Interleukin-1β Production," J. Cell. Biochem., Supplement, 16 pt B:285 (ABSTRACT J216) (1992).
C141	Peters et al., "Vascular Endothelial Growth Factor Receptor Expression During Embryogenesis and Tissue Repair Suggests a Role in Endothelial Differentiation and Blood Vessel Growth," <i>Proc. Nat'l Acad. Sci., USA, 90</i> :8915-8919 (October, 1993).

Examiner	Date	
Signature	Considered	

Sub	estitute for form 1449A/B/P	ro		Complete if Known		
		-	•	Application Number	10/774,802	
IN	<b>NFORMATION</b>	N DI	SCLOSURE	Filing Date	February 9, 2004	
S	TATEMENT	BY A	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
	(Use as many sh	eets as	s necessary)	Examiner Name	To be Assigned	
Sheet	13	of	18	Attorney Docket Number	28967/34891.1	

C142	Pietersz et al., "Antibody Conjugates for the Treatment of Cancer," Immunological Reviews, 129:57-80 (1992).
C143	Plückthun, A. et al., "New protein engineering approaches to multivalent and bispecific antibody fragments," <i>Immunotechnology</i> , 3:83-105 (1997).
C144	Poncz et al., "Cloning and Characterization of Platelet Factor 4 cDNA Derived From a Human Erythroleukemic Cell Line," Blood, 69(1):219-223 (January, 1987).
C145	Rader, C. et al., "Phage display of combinatorial antibody libraries," Curr. Opin. Biotech., 8:503-508 (1997).
C146	Reedijk et al., "Tyr721 Regulates Specific Binding of the CSF-1 Receptor Kinase Insert to P1 3'-Kinase SH2 Domains: a Model for SH2-Mediated Receptor-Target Interactions," EMBO J., 11(4):1365-1372 (1992).
C147	Relf, M. et al., "Expression of the Angiogenic Factors Vascular Endothelial Cell Growth Factor, Acidic and Basic Fibroblast Growth Factor, Tumor Growth Factor β-1, Platelet-derived Endothelial Cell Growth Factor, Placenta Growth Factor, and Pleiotrophin in Human Primary Breast Cancer and Its Relation to Angiogenesis," Cancer Research, 57:963-969 (March, 1997).
C148	Renner, C. et al., "Tumor Therapy by Immune Recruitment with Bispecific Antibodies," <i>Immunological Reviews, No.145</i> , pp. 179-209 (1995).
C149	Riechmann, L. et al., "Reshaping human antibodies for therapy," Nature, 332(6162):323-327 (March, 1988).
C150	Roitt, M., "Essential Immunology," Blackwell Scientific Pub., Oxford, pp.65-68 & 74 (1991).
C151	Rosnet et al., "Isolation and Chromosomal Localization of a Novel FMS-Like Tyrosine Kinase Gene," Oncogene, 6(9):1641-1650 (1991).
C152	Rosnet et al., "Murine Flt3, a Gene Encoding a Novel Tyrosine Kinase Receptor of the PDFR/CSF1R Family," Genomics, 9:380-385 (1991).
C153	Saaristo, A., et al., "Vascular Endothelial Growth Factor-C and its Receptor VEGFR-3 in the Nasal Mucosa and in Nasopharyngeal Tumors," Am. J. Pathology, 157(1):7-14 (July 2000).
C154	Sabin, F.R., "The Lymphatic System in Human Embryos, with Consideration of the Morphology of the System as a Whole," <i>Am. J. Anat.</i> , 9(1):43-91 (1909).

Examiner	Date	
Signature	Considered	

Sub	stitute for form 1449A/B/PT	0		Complete if Known		
		_		Application Number	10/774,802	
IN	<b>IFORMATION</b>	l Di	SCLOSURE	Filing Date	February 9, 2004	
S	TATEMENT B	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
	(Use as many she	eets as	necessary)	Examiner Name	To be Assigned	
Sheet 14 of 18		18	Attorney Docket Number	28967/34891.1		

0455	
C155	Salven, P. et al., "Vascular Endothelial Growth Factors VEGF-B and VEGF-C Are Expressed in Human Tumors," American J. Pathology, 153(1):103-108 (July, 1998).
C156	Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, pp. 2.60-2.70, 4.21-4.32, 7.3-7.36 (1989).
C157	Sato and Seiki, "Regulatory mechanism of 92 kDa type IV collagenase gene expression which is associated with invasiveness of tumor cells," <i>Oncogene</i> , 8:395-405 (1993).
C158	Satoh et al., "Regional Localization of the Human c-ros-1 on 6q22 and flt on 13q12," Jpn. J. Cancer Res., 78:772-775 (1987).
C159	Schneider <i>et al.</i> , "A One-step Purification of Membrane Proteins Using a High Efficiency Immunomatrix," <i>J. Biol. Chem., 257(18)</i> :10766-10769 (September 25, 1982).
C160	Schreiber et al., "Interaction of endothelial cell growth factor with heparin: Characterization by receptor and antibody recognition," Proc. Nat'l Acad. Sci., 82:6138-6142 (September, 1985).
C161	Schwenk et al., "Cell Cycle Dependency of a T-Cell Marker on Lymphoblasts," Blut, 31:299-306 (1975).
C162	Scott, P.A.E. et al., "Laboratory-Clinic Interface: Current approaches to targeting cancer using antiangiogenesis therapies," Cancer Treatment Reviews, 20:393-412 (1994).
C163	Segal, D.M. et al., "Alternative Triggering Molecules and Single Chain Bispecific Antibodies," Journal of Hematotherapy, 4:377-382 (1995).
C164	Segal, D.M. et al., "Targetting of Anti-Tumor Responses with Bispecific Antibodies," <i>Immunobiology</i> , 185(2-4):390-402 (August, 1992).
C165	Sherr et al., "The c-fms Proto-Oncogene Product is Related to the Receptor for the Mononuclear Phagocyte Growth Factor, CSF-1," Cell, 41:665-676 (July, 1985).
C166	Shi et al., "16-Kilodalton Heparin Binding (Fibroblast) Growth Factor Type One Appears in a Stable 40-Kilodalton Complex After Receptor-Dependent Internalization," J. Biol. Chem., 266(9):5774-5779 (March 25, 1991).
C167	Shibuya et al., "Nucleotide Sequence and Expression of a Novel Human Receptor- Type Tyrosine Kinase Gene (flt) Closely Related to the fms Family," Oncogene, 5:519-524 (1990).

Examiner	Date	
Signature	Considered	

Sub	stitute for form 1449A/B/PT	0		Complete if Known		
		_		Application Number	10/774,802	
IN	<b>IFORMATION</b>	l Di	SCLOSURE	Filing Date	February 9, 2004	
S	TATEMENT E	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
	(Use as many she	ets as	necessary)	Examiner Name	To be Assigned	
Sheet 15 of 18		18	Attorney Docket Number	28967/34891.1		

	Shibuya, M., "Role of VEGF-FLT Receptor System in Normal and Tumor Angiogenesis," Advances in Cancer Research, 67:281-316 (1995).	
	Shushanov, S., et al., "VEGFc and VEGFR3 Expression in Human Thyroid Pathologies," Int. J. Cancer, 86:47-52 (2000).	
	Siemeister, et al., "Two independent mechanisms essential for tumor angiogenesis: inhibition of human melanoma xenograft growth by interfering with either the vascular endothelial growth factor receptor pathway or the Tie-2 pathway," Cancer Res. 59:3185-91 (1999)	
	Skobe, M., et al., "Vascular Endothelial Growth Factor-C (VEGF-C) and its Receptors KDR and flt-4 are Expressed in AIDS-Associated Kaposi's Sarcoma," J. Invest. Dermatology, 113:1047-1053 (1999).	
	Sowter, H.M., et al., "Expression and Localization of the Vascular Endothelial Growth Factor Family in Ovarian Epithelial Tumors," Lab. Invest., 77(6):607-14 (December 1997).	
	Stacey et al., "SVpoly: a Versatile Mammalian Expression Vector," Nucl. Acids Res., 18(9):2829 (1990).	
	Staunton <i>et al.</i> , "The Arrangement of the Immunoglobulin-Like Domains of ICAM-1 and the Binding Sites for LFA-1 and Rhinovirus," <i>Cell</i> , 61:243-254 (April 20, 1990).	
	Stenman et al., "Human PDGFA Receptor Gene Maps to the Same Region on Chromosome 4 as the KIT Oncogene," Genes, Chromosomes, Cancer, 1:155-158 (1989).	
	Sundström <i>et al.</i> , "Establishment and Characterization of a Human Histiocytic Lymphoma Cell Line (U-937)," <i>Int. J. Cancer</i> , 17:565-577 (1976).	
	Swolin et al., "On the 5q-Deletion: Clinical and Cytogenetic Observations in Ten Patients and Review of the Literature," Blood, 58:986-993 (1981).	
	Tekmal, R.R. et al., "A novel in vitro and in vivo breast cancer model for testing inhibitors of estrogen biosynthesis and its action using mammary tumor cells with an activated int-5/aromatase gene," Cancer Letters, 118(1):21-28 (September, 1997).	
	Tempest, P.R. et al., "Reshaping a Human Monoclonal Antibody to Inhibit Human Respiratory Syncytial Virus Infection in Vivo," BioTechnology, 9(3):266-271 (March, 1991).	
C180	Terman et al., "Identification of a New Endothelial Cell growth Factor Receptor Tyrosine Kinase," Oncogene, 6(9):1677-1683 (1991).	

		· · · · · · · · · · · · · · · · · · ·
Examiner	Date	
Lamine	Date	
Signature	Considered	
Signature	Considered	

Sub	stitute for form 1449A/B/PT	0		Complete if Known		
		•		Application Number	10/774,802	
11	<b>IFORMATION</b>	I DI	SCLOSURE	Filing Date	February 9, 2004	
S	TATEMENT E	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
	(Use as many she	eets as	necessary)	Examiner Name	To be Assigned	
Sheet 16 of 18		Attorney Docket Number	28967/34891.1			

C181	Terman et al., "Identification of the KDR Tyrosine Kinase as a Receptor for Vascular	
	Endothelial Cell Growth Factor," Biochem & Biophys. Res. Comm., 187(3):1579-1586 (September 30, 1992).	
C182	Thompson <i>et al.</i> , "Cloned Human Teratoma Cells Differentiate into Neuron-Like Cells and Other Cell Types in Retinoic Acid," <i>J. Cell Sci.</i> , 72:37-64 (1984).	
C183	Tomiyasu et al., "Long Arm Deletion of Chromosome No. 5 in a Case of Philadelphia Chromosome-Positive Chronic Myelocytic Leukemia," Cancer Genet. Cytogenet., 2:309-315 (1980).	
C184	Tortora et al., "Differentiation of HL-60 Leukemia By Type I Regulatory Subunit Antisense Oligodeoxynucleotide of a cAMP-Dependent Protein Kinase," Proc. Nat'l Acad. Sci., USA, 88(5):2011-2015 (March, 1991).	
C185	Traunecker, A. et al., "Myeloma based expression system for production of large mammalian proteins," <i>Trends in BioTechnology</i> , 9(4):109-113 (April, 1991).	
C186	Tsurusaki, T., et al., "Vascular endothelial growth factor-C expression in human prostatic carcinoma and its relationship to lymph node metastasis," Br. J. Cancer, 801(2):309-313 (1999).	
C187	Ullrich et al., "Signal Transduction By Receptors with Tyrosine Kinase Activity," Cell, 61:203-212 (April 20, 1990).	
C188	Valtola, R., et al., "VEGFR-3 and Its Ligand VEGF-C Are Associated with Angiogenesis in Breast Cancer," Am. J. Pathol., 154(5):1381-90 (May 1999).	
C189	Van der Putte, S.C.J., "The Development of the Lymphatic System in Man," Adv. Anat. Embryol. Cell Biol., 51:3 (1975).	
C190	Van Den Berghe <i>et al.</i> , "Distinct Haematological Disorder with Deletion of Long Arm of No. 5 Chromosome." <i>Nature, 251:</i> 437-439 (1974).	
C191	Van Den Berghe et al., "Transformation of Polycythemia Vera to Myelofibrosis and Late Appearance of a 5q-Chromosome Anomaly," Cancer Genet. Cytogenet., 1:157-162 (1979).	
C192	Van Hinsberg et al., "Effect of Thrombin on the Production of Plasminogen Activators and PA Inhibitor-1 by Human Foreskin Microvascular Endothelial Cells," <i>Thromb. Haemostas.</i> , 57(2):148-153 (1987).	
C193	Van Hinsberg et al., "Production of Plasminogen Activators and Inhibitors by Serially Propagated Endothelial Cells From Adult Human Blood Vessels," Arteriosclerosis, 7:389-400 (July/August, 1987).	

Examiner		Date	
Signature		Considered	

Sut	estitute for form 1449A/B/PT	0		Complete if Known		
				Application Number	10/774,802	
11	<b>IFORMATION</b>	I DI	SCLOSURE	Filing Date	February 9, 2004	
S	TATEMENT E	<b>3Y</b> /	APPLICANT	First Named Inventor	Kari Alitalo et al.	
				Art Unit	1646	
	(Use as many she	eets as	necessary)	Examiner Name	To be Assigned	
Sheet 17 of 18		18	Attorney Docket Number	28967/34891.1		

Tare:	
C194	Verhoeyen, M. et al., "Reshaping Human Antibodies: Grafting an Antilysozyme Activity," Science, 239:1534-1536 (March, 1988).
C195	Voet, et al., Biochemistry, John Wiley & Sons, Inc., pages 126-128 and 228-234, 1990.
C196	Wang, "Signal Transduction in Human Hematopoietic Cells by Vascular Endothelial Growth Factor Related Protein, a Novel Ligand for the FLT4 Receptor," Blood, 90(9):3507-3515 (November, 1997).
C197	Warrington et al., "Radiation of Hybrid Map of 13 Loci on the Long Arm of Chromosome 5," Genomics, 11:701-708 (1991).
C198	Weidner, N. et al., "Tumor Angiogenesis: A New Significant and Independent Prognostic Indicator in Early-Stage Breast Carcinoma," J. Natl. Cancer Inst., 84(24):1875-1887 (December, 1992).
C199	Wen, D. et al., "New Differentiation Factor: A Transmembrane Glycoprotein Containing an EGF Domain and an Immunoglobulin Homology Unit," Cell, 69:559-572 (May 1, 1992).
C200	Weninger, W., et al., "Expression of Vascular Endothelial Growth Factor Receptor-3 and Podoplanin Suggests a Lymphatic Endothelial Cell Origin of Kaposi's Sarcoma Tumor Cells," Lab. Invest., 79(2):243-51 (February 1999).
C201	Whang-Peng et al., "Cytogenic Studies in Patients With Myelofibrosis and Myeloid Metaplasia," Leuk. Res., 2:41-48 (1978).
C202	Wilkinson <i>et al.</i> , "Expression of the Proto-Oncogene int-1 is Restricted to Specific Neural Cells in the Developing Mouse Embryo," <i>Cell</i> , 50:79-88 (1987).
C203	Williams et al., "The Immunoglobin Superfamily-Domains for Cell Surface Recognition," Ann. Rev. Immunol., 6:381-405 (1988).
C204	Williams, J.C. et al., "N-methyl-N-nitrosourea-Induced Rat Mammary Tumors. Hormonal Responsiveness but Lack of Spontaneous Metastasis," J. Nat. Cancer Inst., 66(1):147-155 (January, 1981).
C205	Witmer, et al., "VEGFR-3 in adult angiogenesis," J. Path. 195:490-497 (2001)
C206	Witzenbichler, B., et al., "Vascular Endothelial Growth Factor-C (VEGF-C/VEGF-2) Promotes Angiogenesis in the Setting of Tissue Ischemia," American Journal of Pathology, Vol. 153, No.2:381-394 (August 1998).
C207	Yamaguchi et al., "Flk-1, an Flt-Related Tyrosine Kinase is an Early Marker for Endothelial Cell Precursors," Development., 118:489-498 (1993).

Examiner		Date	
Signature	•	Considered	

Substitute for form 1449A/B/PTO				Complete if Known	
		_		Application Number	10/774,802
INFORMATION DISCLOSURE				Filing Date	February 9, 2004
S	TATEMENT E	3Y /	APPLICANT	First Named Inventor	Kari Alitalo et al.
				Art Unit	1646
	(Use as many she	eets as	s necessary)	Examiner Name	To be Assigned
Sheet	18	of	18	Attorney Docket Number	28967/34891.1

C208	Yarden et al., "Human Proto-Oncogene c-kit: A New Cell Surface Receptor Tyrosine Kinase for an Unidentified Ligand," EMBO J., 6(11):3341-3351 (1987).
C209	Ylänne et al., "Platelet Glycoprotein IIb/IIIa Complex in Cultured Cells: Localization in Focal Adhesion Sites in Spreading HEL Cells," Blood, 72: 1478-1486 (1988).
C210	Yokoyama, Y., et al., "Prognostic Significance of Vascular Endothelial Growth Factor and Its Receptors in Endometrial Carcinoma," Gyn. Oncology 77:413-418 (2000).
C211	Yonemura, Y., et al., "Role of Vascular Endothelial Growth Factor C Expression in the Development of Lymph Node Metastasis in Gastric Cancer," Clin. Cancer Res., 5:1823-1829 (July 1999).

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Examiner	Date
Signature	Considered

<sup>&</sup>lt;sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.